Pigmentation of Osteoma Cutis
Caused by Tetracycline

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Blue nodules developed in the skin of a patient with acne concomitant with the start of tetracycline therapy. When removed, these nodules were brown and histologic examination revealed a lamellate structure compatible with bone. Under ultraviolet light, these osteomas fluoresced yellow, indicating the presence of tetracycline. This suggests that tetracycline, combined with new bone formation, causes pigmentation of osteoma cutis. (Arch Dermatol 115:1087-1088, 1979)

Osteoma cutis was first reported to occur with acne vulgaris by Hopkins in 1928. Subsequently, Leder reported a number of cases in the period from 1948 to 1951. Clinically, these osteomas were either small white nodules in the skin or were clinically inapparent and demonstrable only on soft-tissue x-ray examination. More recent reports of facial osteomas point out the coloration of these nodules, which is a change from earlier reports. We describe a patient with cutaneous blue osteomas that developed while the patient was receiving tetracycline therapy. When removed from the skin, these osteomas were brown and fluoresced yellow under ultraviolet light. This suggests that tetracycline, combined with new bone formation, causes pigmentation of osteoma cutis.

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Fig 1.—Pigmented osteoma cutis scattered over face, especially forehead and temples.
Fig 2.—Closer view of forehead showing characteristic "blue dots" seen with this disorder.
Fig 3.—Histologic findings of pigmented nodule reveal bony structure made of concentric lamellate rings with lacunae, many of which contain nuclei. Hair follicles and sebaceous glands appear displaced (decalcified, hematoxylin-eosin, original magnification x16).
Fig 4.—Ultraviolet lamp examination of pigmented osteomas from patient (left), untreated human bone chips (center), and human bone chips dipped in 1% tetracycline hydrochloride aqueous solution (right). Note yellow fluorescence of pigmented osteomas and tetracycline-dipped bone chips as compared to untreated human bone chips.
bone formation, is the cause of the pigment in these osteomas.

REPORT OF A CASE

A 21-year-old woman had a four-year history of blue nodules over her face (Fig 1 and 2) and the upper part of her chest. She had had acne vulgaris since 15 years of age and was first treated with 250 mg of tetracycline orally twice a day on an intermittent basis over a two-year period when she was 17 years old. Shortly after starting tetracycline therapy, she noted the development of small "blue dots" in her skin. She was able to remove a few of these herself and observed that they were like "little rocks."

A 3-mm punch biopsy specimen demonstrated that these nodules were indeed osteomas. Histologic examination of a decalcified specimen revealed a bony structure containing concentric lamellate rings with lacunae, many of which contained nuclei (Fig 3). Surrounding the osteoma were hair follicles and sebaceous glands that appeared to be displaced. The nodules could be expressed from the skin with the tip of a scalpel blade and clinically appeared as 1- to 3-mm brown spherical grains. These pigmented osteomas were examined for fluorescence with a lamp that emits ultraviolet light primarily at a wavelength of 365 nm. A yellow fluorescence was apparent and was similar to that seen with normal human bone chips dipped in an aqueous solution containing 1% tetracycline hydrochloride (Fig 4).

Approximately 75 osteomas were subsequently removed from the patient over five treatment periods, resulting in marked cosmetic improvement without scarring. To date, no pigmented osteomas have recurred; the patient is not receiving tetracycline therapy. Her acne was controlled with topical 10% benzoyl peroxide gel and 0.025% tretinoin. Serum calcium and phosphorus levels were normal.

COMMENT

Multiple small osteomas of the skin were described as early as 1864 by Virchow. Subsequent reports of osteomas occurring in acne vulgaris emphasized that this was probably metastastic bone formation occurring in areas of calcium deposits secondary to inflammatory skin damage. X-ray diffraction analysis has shown that the crystalline component of these osteomas is hydroxyapatite, a primary constituent of true bone. Up to 50% of patients with acne may show radiopaque densities on soft-tissue x-ray examination of the face. The majority of these densities may represent calcium deposition and only a small percentage osteomas. Clinically, these densities are usually not detectable either visually or by palpation. However, since tetracycline was introduced in 1952, there have been reports of blue-pigmented osteomas developing mainly in patients with acne who received tetracycline or antibiotics of an unspecified type. In only one case was tetracycline or antibiotic therapy given for systemic effect not mentioned as part of the patient’s previous treatment. Tetracycline is known to form a complex with calcium orthophosphate and can be deposited in developing teeth and bone. In children, this can lead to brown discoloration of the permanent anterior teeth if tetracycline is given between 6 months and 5 years of age. The color appears to depend on the amount of tetracycline given, and under ultraviolet light the teeth fluoresce yellow. Since cutaneous osteomas represent new bone formation, tetracycline given during their development can result in brown discoloration. Because brown pigment in the dermis absorbs red rays and reflects blue rays, these brown osteomas appear blue in the skin.

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Nonproprietary Names and Trademarks of Drugs

Benzoyl peroxide—Benzaigel, Desquam-X, Oxy-5, Panoyzil, Persa-Gel, Persadox.
Tetracycline—Achromycin V Syrup, Pediatric Drops; Panmycin; SK-Tetracycline; Tetracyn.

References